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This document details the final determination regarding the the Rebuttable Presumption Against Registration (RPAR) of products containing the above chemical. The responses by by EPA to comments on the preliminary determination by the Scientific Advisory Panel and the United States Department of Agriculture are contained in the document. A bibliography of citations used in this final determination is also provided.

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OXYFLUORFEN
POSITION DOCUMENT

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Oxyfluorfen
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Executive Summary

Oxyfluorfen (Goal 2E) was referred for Rebuttable Presumption Against Registration (RPAR) review in January, 1980, because pesticide products containing oxyfluorfen were shown to be contaminated with perchloroethylene (PCE), a demonstrated liver carcinogen in B6C3F1 mice. The review was initiated because of the potential for human risk via dietary and applicator exposure.

Goal 2E is the only registered product containing oxyfluorfen. It is registered as a herbicide for both pre-emergence and post emergence control of certain weed species on conifer seedbeds and transplants, bearing and nonbearing tree fruits and nuts, soybeans and field corn (USDA Witchweed Eradication Program). The sole producer and registrant is the Rohm and Haas Company of Philadelphia, Pennsylvania.

In March 1981, the Agency issued a position document integrating the presumption against registration and the risk/benefit analysis (position document 1/2/3). In this document, the Agency proposed to limit the level of the PCE contaminant to 200 ppm or less. This reflected the level the registrant had stated was both economically and technically feasible. Risks estimated by the Agency at the 200 ppm level for the PCE contaminant were not large and were considered to be outweighed by the benefits of the use of oxyfluorfen.

The risk estimate for applicators was based on a very conservative model of inhalational exposure rather than actual field measurements. Because of the risk estimates associated with this model, the Agency proposed to require, within six months of the final decision, the use of respirators by mixer/loader/ applicators for currently registered and proposed uses to reduce inhalational exposure, unless the registrant submitted actual monitoring data showing levels of inhalational exposure significantly lower than those estimated.

The Agency recommended in the PD 1/2/3 the continuation of registration for use on conifers and nonbearing tree fruits and nuts, since the relatively small risks to applicators for these uses were determined to be exceeded by the benefits.

The pending registration actions for Goal at the initiation of the RPAR review were for soybeans, field corn and bearing tree fruits/nuts. The recommended decision in the PD 1/2/3 was to approve these proposed registrations on condition that the registrant provide necessary data required to support full registration. These conditional registrations were subsequently approved.

During this review, the Agency also determined that for uses of Goal, data are currently inadequate to properly assess certain possible adverse effects of oxyfluorfen itself. These possible adverse effects include oncogenicity, mutagenicity, teratogenicity, persistence and bioaccumulation in the aquatic environment, and avian reproduction. The request for these data is independent of the Agency's RPAR determination. The registrant is currently engaged in discussions with the Agency concerning these data requirements.

The Agency also determined that the risk to aquatic plants, aquatic invertebrates, wildlife and fish from all uses of oxyfluorfen could be reduced by labeling without adverse impact on benefits. For the soybean use, additional labeling to protect certain species of endangered aquatic molluscs from the possible hazard posed by the erosion of oxyfluorfen-bound soil was proposed. The registrant has subsequently filed label amendments to include these changes.

The Scientific Advisory Panel and the United States Department of Agriculture have both concurred on the proposed decision in the PD 1/2/3. Their comments on the auxiliary issues have been addressed in the PD 4.

The Agency has decided that the final determination regarding oxyfluorfen will remain unchanged from that proposed in the PD 1/2/3.

I. Introduction

Under the Federal Insecticide, Fungicide, and Rodenticide Act, as amended (FIFRA) (7 U.S.C. Section 136 et seq) the Environmental Protection Agency (EPA or the Agency) regulates all pesticide products. Section 6(b) of FIFRA authorizes the Administrator of the EPA to issue a notice of intent to cancel the registration of a pesticide or to change its classification if it appears to him that the pesticide or its labeling "does not comply with the provisions of [FIFRA] or, when used in accordance with widespread and commonly recognized practice, generally causes unreasonable adverse effects on the environment" Section 3(c)(6) authorizes the Administrator to deny applications for pesticide registration if the statutory standards for registration are not met.

The Agency designed the Rebuttable Presumption Against Registration (RPAR) process to gather risk and benefit information about problem pesticides and to make balanced decisions concerning them in a manner which allows all interested groups to participate. This process is set forth in 40 CFR 162.11.

A. Summary of Position Document 1/2/3

Oxyfluorfen was referred to the Special Pesticide Review Division of the Office of Pesticide Programs in January of 1980 because pesticide products containing oxyfluorfen as an active ingredient are contaminated with perchloroethylene (PCE). PCE was demonstrated to be a liver carcinogen in mice in a National Cancer Institute (NCI) carcinogenicity bioassay (1977). Because of the carcinogenic potential of PCE shown in the NCI study, the Agency determined that PCE-contaminated oxyfluorfen met or exceeded the rebuttable presumption against registration (RPAR) criterion for oncogenicity as set forth in 40 CFR 162.11.

In the interest of achieving an expedited review of the uses of oxyfluorfen, the Agency decided to issue a position document which integrated the position document 1 presumption against registration and the position document 2/3 risk/benefit analysis. It seemed reasonable to focus public discussion on the risk/benefit analysis by presenting the Agency's proposed position in a single document, the Position Document 1/2/3, (PD 1/2/3).

Currently, there is one registered product containing the active ingredient oxyfluorfen. This product is marketed under the trade name Goal® 2E, contains 23.5 percent oxyfluorfen, and, along with technical oxyfluorfen, is manufactured solely by the Rohm and Haas Company of Philadelphia, Pennsylvania.

At the initiation of this review, Goal® 2E had already been registered for use on conifer seedbeds, transplants and outplantings, and certain nonbearing tree fruits/nuts in California; and conditional registrations were pending for soybeans, certain bearing tree fruits/nuts and field corn. The field corn use applies only to those 38 counties in North and South Carolina which are part of the U.S. Department of Agriculture Witchweed Eradication Program. The conditional registrations were subsequently granted in an action separate from the PD 1/2/3, with the conditions described in the PD 1/2/3.

1. Risk

Based upon "worst case" exposure situations and the current maximum level of PCE in formulated oxyfluorfen products (200 ppm), the Agency estimated the carcinogenic risk associated with PCE-contaminated oxyfluorfen to both the agricultural worker and the general public.

The carcinogenic risk associated with each of the uses of PCE-contaminated oxyfluorfen is presented in Table 1. These values show slightly higher levels of risk than those presented in the PD 1/2/3. This discrepancy is discussed further in Section II of this document.

Five other areas of concern were also addressed in the PD 1/2/3, related to oxyfluorfen itself. The areas of concern were oncogenicity, mutagenicity, teratogenicity, and subchronic effects. The potential for adverse environmental effects was also examined in light of the pending registrations for the corn and soybean uses. Valid data concerning the chronic toxicity of oxyfluorfen in the above-mentioned categories are necessary to support registration of all uses of oxyfluorfen.

2. Benefits

The benefits associated with each use of oxyfluorfen were discussed at length in the PD 1/2/3. In summary, the benefits of oxyfluorfen use include the following.

- Oxyfluorfen possesses both pre- and post emergence activity. This increases herbicide utility and allows for season-long control of certain weeds.
- Oxyfluorfen is less dependent on soil and moisture conditions than some otherwise comparable herbicides.
- Oxyfluorfen appears to be uniquely effective for control of certain problem weeds (e.g. cheeseweed, witchweed).
- Oxyfluorfen is competitively priced with respect to other herbicides registered for the same use pattern.
- Oxyfluorfen, when applied as directed, will not cause injury to conifers or crops specified on the label.

3. Risk/Benefit Analysis and Regulatory Options

The Agency developed various regulatory options with respect to oxyfluorfen products and has evaluated each option for its impact on risks and benefits.

The regulatory options considered in the PD 1/2/3 for conclusion of the oxyfluorfen RPAR focused on methods to reduce levels of human exposure to the PCE contaminant, and to reduce environmental risk associated with the uses of oxyfluorfen.

Table 1

Carcinogenic Risk[a/] to Agricultural Workers and to the General Population Associated with the Use of PCE[b/]-Contaminated Oxyfluorfen.

CROP	RISK	
	Worker (Inhalational + Dermal)[c/]	General Public (Dietary)
Soybeans	4.20×10^{-6}	5.30×10^{-8}
Field Corn	1.10×10^{-4}	3.03×10^{-8}
Tree Fruits/Nuts	1.70×10^{-5}	1.00×10^{-6}
Conifers	1.80×10^{-5}	------

a/ Based on multistage model.

b/ Assumes 200 ppm in formulated product.

c/ Inhalation is estimated to be the primary route of exposure. See revised Table 4.

The Agency considered the following six regulatory options.

a. Specify a maximum PCE contamination level of 200 ppm in formulated oxyfluorfen products.

b. Require protective equipment (suitable respirators) to be worn during the mixing, loading, and application of oxyfluorfen products.

c. For the pending registration for soybean use, prohibit use of oxyfluorfen products in counties providing habitat for endangered molluscs.

d. Require labeling for the pending registration for soybean use in order to protect aquatic molluscs.

e. Require labeling for all uses of oxyfluorfen for the protection of aquatic plants, aquatic invertebrates, wildlife and fish.

f. Require development of certain data on the possible adverse effects of oxyfluorfen on man and the environment to be submitted to the Agency by the registrant. The areas of concern for which the data would be required include: oncogenicity, mutagenicity, teratogenicity, subchronic effects, persistence and bioaccumulation in the environment, and toxicity to fish and wildlife.

The risks and benefits for each use were compared under each appropriate option listed above. This use-by-use risk/benefit analysis was detailed in the PD 1/2/3.

4. Proposed Regulatory Decision

Based on the use-by-use risk/benefit analysis, the Agency proposed the following regulatory decision.

For all uses of oxyfluorfen products (currently registered and proposed) the Agency proposed that:

- The PCE contamination of formulated oxyfluorfen products (Goal® 2E) may not exceed 200 ppm and that a statement to that effect be added to the confidential statement of formula for each registered oxyfluorfen product.

- A pesticide respirator jointly approved by the Mining Enforcement and Safety Administration (formerly the U.S. Bureau of Mines) and by the National Institute for Occupational Safety and Health under the provisions of 30 CFR Part II for perchloroethylene must be used during the mixing, loading and application of all oxyfluorfen products. Labelling of all oxyfluorfen products must be amended to include this statement. This requirement will take effect six months after the date of publication of the Notice announcing the final determination concluding the oxyfluorfen RPAR, unless by that time the registrant submits field monitoring data to the Agency establishing that the inhalational exposure for the maximum application rate for each registered use is significantly lower than the inhalational exposure estimated by the Agency.

- Labeling for the protection of wetlands and other aquatic resources is required as part of the conditions for registration. Specific label statements are to read as follows.

  For Soybeans:

  "This product is highly toxic to freshwater clams, oysters, aquatic invertebrates and aquatic plants. Do not apply where visible erosion to aquatic habitats and wetlands occurs."

  For all other uses:

  "This pesticide is highly toxic to aquatic plants, aquatic invertebrates, wildlife and fish. Use with care when applying in areas frequented by wildlife or adjacent to any body of water or wetland area. Do not apply when weather conditions favor drift or erosion from target area. Do not contaminate water bodies by cleaning of equipment or disposal of wastes."

The Agency also determined that with the adoption of the above-mentioned provisions, amending the existing Goal 2E registration to include use on soybeans, field corn, and bearing tree fruits/nuts would not significantly increase the risk of unreasonable adverse effects on man or the environment. The Agency, however, recommended that subsequent registrations for these proposed uses (field corn, soybeans, bearing tree fruits/nuts and any other uses to be proposed) include the following condition due to oxyfluorfen's persistence and potential to bioaccumulate.

> Extensive field monitoring for oxyfluorfen residues in each proposed use pattern area would be required. The registrant would submit these data to the Agency within two years of the date of conditional registration.

The detailed rationale for the proposed decision is presented in the PD 1/2/3. In summary, those options which would result in maximum risk reduction or incremental risk reduction with minimum impact on the benefits of oxyfluorfen use. During the course of this review the registrant reduced the PCE contamination of oxyfluorfen from 1680 ppm to 200 ppm or less in the formulated product. The Agency based its risk assessment on the current level (200 ppm) of PCE in oxyfluorfen and "worst case" exposure conditions. Based on the resulting "worst case" risk figures, the Agency determined that to allow PCE levels higher than 200 ppm would increase the risk without a concomitant increase in benefits. Limiting PCE levels to 200 ppm would not affect the benefits adversely, because oxyfluorfen is currently produced with levels of 200 ppm or less PCE.

The "worst case" exposure estimates resulted in risk estimates for mixer/loader/applicators which the Agency believed warranted the use of protective equipment. Because inhalational exposure appears to be the major component of worker risk, respirators would be required unless actual monitoring data submitted by the registrant demonstrate that exposure to PCE during application of oxyfluorfen is significantly less than that estimated by the Agency. This course of action will reduce risk, not adversely affect the benefits, and provide the registrant with the option of supplying additional information to the Agency so that the risk assessment and consequently the regulatory decision may be modified as indicated by these data.

The environmental hazard labeling, as part of the conditions for registration, is designed to reduce the possible hazard to the environment, in particular to aquatic habitats, without major use restrictions. For the soybean use pattern, specific labeling has been developed. This labeling has been coupled with a requirement for extensive field monitoring for oxyfluorfen residues. If levels in aquatic habitats are found in monitoring studies to approach toxic levels, the Agency may reconsider the option of restricting use of oxyfluorfen from those counties providing habitat for endangered molluscs. This monitoring requirement has also been required as a condition of registration for the field corn and tree fruit/nut uses.

In an action independent of the RPAR under authority of FIFRA section 3(c)(2)(B), the Agency stated in the PD 1/2/3 that the registrant would be required to submit the following oxyfluorfen studies to the Agency in support of all registrations.

- The registrant is to be required to submit to the Agency an oxyfluorfen teratogenicity study in rabbits. The protocol of this study should include post-natal evaluation and should be submitted before initiation of testing.

- A battery of mutagenicity tests are to be submitted to the Agency. Protocols should be submitted to the Agency prior to the initiation of testing.

- The registrant is to be required to submit an oxyfluorfen oncogenicity study in mice and an oxyfluorfen oncogenicity study in rats. Protocols for these studies are to be submitted prior to initiation of testing.

- The registrant is to be required to submit a 6-month (or longer) dog feeding study which demonstrates a no-observed-effect level (NOEL). Protocols for this study have been published in 43 FR 37536, August 22, 1978.

- The registrant is to be required to submit avian reproduction studies with mallard ducks and bobwhite quail.

The registrant is currently engaged in discussions with the Agency concerning these proposed actions for testing of oxyfluorfen. In the course of these discussions, the Agency has determined that the information needed to evaluate the human health effects of oxyfluorfen can be obtained without requiring the registrant to perform all of the studies specifically detailed in the PD 1/2/3. As a result of clarification of data in the existing dog chronic feeding study, the Agency has found the study demonstrates an acceptable no-observed-effect level and the registrant will not be required to repeat the study. The Agency has also determined that, since the acceptability of earlier rodent oncogenicity studies hinges on whether the highest experiment dose was near the maximum tolerated dose (MTD), the registrant will first conduct short-term studies to determine the MTD. Unless this MTD is significantly higher than the

high dose in the earlier experiments, the Agency will not require further oncogenicity testing. All proposed testing requirements are currently under discussion with the registrant. Final determination of the studies to be required will be made when discussions with the registrant are completed, and the Agency will issue a letter to the registrant, under authority of FIFRA section 3(c)(2)(B), requesting the studies. At that time, the Agency will specify a value of the NOEL for teratogenicity data that indicates acceptable safety, based on calculated exposure and an adequate magin of safety.

B. Request for Comments

FIFRA requires the Agency to submit notices issued pursuant to section 6 to the Secretary of Agriculture for comment on the proposed action [section 6(b)] and to a Scientific Advisory Panel (SAP) for comment on the impact of the proposed action on health and the environment [section 25(d)]. The Secretary of Agriculture and SAP are invited to comment, as required by the statute, in writing within 30 days of receiving the notice and the Agency is required to publish their comments and the Administrator's response with publication of the notice of final determination.

The Agency presented its proposed decision to the SAP at a public meeting held on May 13 and 14, 1981. Notice of the meeting was published in the Federal Register on April 27, 1981, indicating the availability of the PD 1/2/3 and describing the procedures for making oral and written comments. In addition, the SAP contacted, by mail, members of the general public who had previously expressed an interest in the Panel's activities. The SAP meeting was attended by the registrant and other interested parties.

The Agency has received three sets of comments in response to the March, 1981, Oxyfluorfen Position Document 1/2/3. Responses from the SAP, the U.S. Department of Agriculture, and the registrant have been analyzed and are addressed in Section III of this document. The responses from the SAP and the USDA are presented in Appendix B in their entirety.

II. Revisions and Amendments to PD 1/2/3 - Exposure and Risk

Since publication of the PD 1/2/3, the estimates of PCE exposure have been revised. Refinements in calculation have demonstrated that exposure to PCE from use of oxyfluorfen products had been underestimated by a factor of three in the initial review. As a result, it was also necessary to revise the risk figures, which are a function of the exposure.

Tables 2 and 3 present the original and revised PCE exposure estimates for all uses of oxyfluorfen. Revised risk estimates are presented in Table 4. All tables relating to exposure and risk estimates which were presented in the PD 1/2/3 have been corrected and the revised editions appear in Appendix A of this document.

From a review of Tables 2, 3, and 4, of this document, the Agency concludes that the revised risk figures are not significantly different from those which appear in the PD 1/2/3. However, the Agency wishes to present the most accurate evaluation possible in its final decision. The Agency has determined that these revisions do not affect the proposed regulatory action. The means for reducing risk to applicators have already been proposed, and these are sufficient to take into account the slightly higher revised risk figures.

Table 2

Adjusted Lifetime Average Daily Worker Exposure to PCE[a] from Use of Oxyfluorfen[b]

Route	Crop	Exposure[c] (mg/kg/day)	
		Original	Revised
Inhalational[d]	Soybeans	0.3×10^{-4}	0.8×10^{-4}
	Field corn	7.0×10^{-4}	20.6×10^{-4}
	Tree fruits/nuts	1.1×10^{-4}	3.3×10^{-4}
	Conifers	1.1×10^{-4}	3.3×10^{-4}
Dermal[e]	Soybeans	0.4×10^{-6}	1.2×10^{-6}
	Field corn	20.0×10^{-6}	60.0×10^{-6}
	Tree fruits/nuts	0.4×10^{-6}	1.3×10^{-6}
	Conifers	1.7×10^{-6}	4.8×10^{-6}
Total	Soybeans	0.3×10^{-4}	0.8×10^{-4}
	Field corn	7.2×10^{-4}	21.0×10^{-4}
	Tree fruits/nuts	1.1×10^{-4}	3.3×10^{-4}
	Conifers	1.1×10^{-4}	3.4×10^{-4}

a/ Assumes 200 ppm in formulated product.

b/ Assumes exposure time of 10 days/year (62.5 days for corn), a working life of 40 years and a 70-year life span.

c/ See Appendix A, Tables 2 and 3 for individual daily dermal and inhalation figures.

d/ Based on an 8-hour day of spraying.

e/ Based on 1 hour mixing/loading and 7-hours spraying.

Table 3

Adjusted Maximum Dietary Exposure to PCE[a] from Uses of Oxyfluorfen

Crop	Exposure[b] (mg/kg/day)	
	Original	Revised
Soybean	1.04×10^{-6}	1.04×10^{-6}
Field Corn	0.05×10^{-6}	0.57×10^{-6}
Tree Fruit/Nuts	19.00×10^{-6}	19.00×10^{-6}

a/ Assumes that 0.05 ppm level of analytical sensitivity is equivalent to 0.05 mg/kg of commodity.

b/ Daily consumption of commodity in mg/person/day based on average consumption figures for each commodity (U.S. EPA, 1981, PD 1/2/3).

Table 4

Carcinogenic Risk[a/] to Agricultural Workers and the General Public Associated with the Uses of PCE[b/]-Contaminated Oxyflurofen

Crop	Risk Estimate	
	Original	Revised[c/]
WORKER:		
Soybean	1.5×10^{-6}	4.2×10^{-6}
Field Corn	3.8×10^{-5}	1.1×10^{-4}
Tree Fruits/Nuts	5.8×10^{-6}	1.7×10^{-5}
Conifers	5.8×10^{-6}	1.8×10^{-5}
DIETARY:		
Soybeans	5.30×10^{-8}	5.30×10^{-8}
Field Corn	2.65×10^{-9}	3.03×10^{-8}
Tree Fruits/Nuts	1.00×10^{-6}	1.00×10^{-6}

a/ Uses multistage model for calculations.

b/ Assumes 200 ppm PCE in formulated product.

c/ Uses revised exposure figures from Tables 2 and 3.

III. Analysis of Comments

The Agency received comments from the Secretary of Agriculture, the Scientific Advisory Panel (SAP) and the registrant. These comments are organized by topic and discussed below. As indicated in the following discussion, the Agency has revised some aspects of its assessment of risks, benefits, and regulatory requirements in accordance with USDA, SAP, and other recommendations. Except as discussed below and in Section II, other aspects of the analysis presented in the Position Document 1/2/3 are unchanged.

A. Comments Relating to Risk

The Agency has received no comments on its assessment of the carcinogenic risk from PCE associated with the uses of oxyfluorfen. Minor revisions in exposure and risk figures have been made by the Agency and have been presented and discussed in Section II of this document.

The SAP has concurred with the Agency's assessment of risk from PCE but has stated that it has "a number of serious concerns with oxyfluorfen not related to the oncogenic hazard from PCE..." (30000/36:#3). These concerns relate to the following issues.

1. The persistence and possible bioaccumulation of oxyfluorfen in the food chain.

2. The adequacy of testing of oxyfluorfen's potential teratological effects given its structural resemblance to nitrofen.

3. The identification and potential adverse effects of the various inert ingredients in oxyfluorfen.

With regard to issue (1) above, the Agency shares the SAP's concern regarding the persistence of oxyfluorfen in the environment. This concern was discussed in the PD 1/2/3 and the Agency has proposed that extensive field monitoring for oxyfluorfen residues in the major use pattern areas be required as part of the conditions for registration. The field monitoring outlined by the Agency in the PD 1/2/3 includes provisions for evaluating the potential of oxyfluorfen to bioaccumulate in aquatic organisms.

Issue number (2) pertains to oxyfluorfen's potential to cause teratogenic effects. This concern arises from the fact that oxyfluorfen is structurally similar to nitrofen, a known teratogen. Therefore, the SAP believes that an especially careful evaluation of oxyfluorfen is warranted.

The Agency agrees with the SAP that a special effort should be made to determine that no teratological problem exists with oxyfluorfen. The PD 1/2/3 discussed the information available at the time and highlighted the need for some further study. Along with the rat teratology study submitted by the registrant (negative for teratogenic effects at 1000 mg/kg/day), the registrant is currently conducting a second teratology study with rabbits which will be submitted in late 1981. Additional teratogenic evaluation of oxyfluorfen is being conducted by EPA at its Research Triangle Park (RTP), N.C. facility. The EPA scientist in charge of this research has also evaluated the teratogenic effects of nitrofen and acifluorfen (two diphenyl ethers similar to

oxyfluorfen). Therefore, any teratogenic effects of oxyfluorfen similar to those of nitrofen should be recognized. Also, the Agency points out that structurally similar chemicals do not necessarily possess the same toxicological characteristics. Evidence of this in the case of diphenyl ethers comes from the above-mentioned EPA studies being done at RTP. Data from these studies indicate that nitrofen is teratogenic but that acifluorfen is negative for teratogenic effects (Dykstra, 1981).

Following the evaluation of the rabbit teratology study, to be submitted in late 1981 by the registrant, and the results of EPA testing of oxyfluorfen, the Agency will then determine whether further testing is warranted, or whether the information to date is sufficient to accurately evaluate the teratogenic potential of oxyfluorfen.

SAP's third concern relates to the level of impurities in technical oxyfluorfen and the possible adverse effects of these impurities on the environment.

Although not specifically discussed in the PD 1/2/3, the identification of and toxicological information on the impurities in technical oxyfluorfen have been submitted to and reviewed by the Agency (Rohm and Haas, 1978; Perfetti, 1978; and Dykstra, 1978). Unless an impurity or inert ingredient of a pesticide is judged to pose an unreasonable adverse effect on man or the environment, it is illegal to disclose such product information in a public document. The Agency has addressed the issue of the impurities in technical oxyfluorfen and the relevant reviews are on file. These reviews were provided to the SAP. The panel expressed their satisfaction with the adequacy of these reviews.

B. Comments Relating to Benefits

The only comments relating to oxyfluorfen benefits were received from USDA (30000/36:#2). Essentially, the USDA concurs with the Agency assessment of benefits and adds that oxyfluorfen is particularly beneficial for witchweed control and use in forest nurseries. The Agency agrees and believes that the benefits of oxyfluorfen for use in corn and forest nurseries have been adequately discussed in the PD 1/2/3.

C. Comments Relating to Regulatory Options - Respirator Requirement for Mixer/Loader/Applicators

The USDA (30000/36:#2) has agreed with the Agency's proposal to require respirators during the mixing, loading, and application of oxyfluorfen products. The USDA commented, however, that this requirement does not take into account different methods of application. The USDA stated that in many forest nurseries, pesticides are applied through automatic watering systems which would result in little or no applicator exposure.

In assessing applicator exposure to PCE from use of oxyfluorfen products, the Agency assumed spray application as indicated on the Goal® 2E conifer label. The Goal® 2E label does not currently provide rates, metering instructions, limitations, precautions or other directions for use of Goal® 2E through automatic watering systems. As indicated in the PD 1/2/3, oxyfluorfen performance and exposure data are extremely limited.

The USDA also commented that use of respirators in many areas of the United States poses problems of discomfort due to heat and humidity and that in certain high temperature situations the hazards associated with the use of respirators may be more immediate and dangerous than the hazard due to pesticide exposure. The USDA suggests that research is needed to devise protective measures suitable for hot weather.

In the case of oxyfluorfen, inhalational exposure accounts for 98 percent or more of the total applicator exposure to the PCE contaminant, according to Agency estimates. Reducing inhalational exposure is therefore the most effective method of reducing total exposure of applicators to PCE in oxyfluorfen. Respirator use dramatically decreases total exposure and resultant risk, as illustrated in revised Table 11.

The Agency recognizes the reluctance of applicators to wear respirators in hot and humid weather situations. The Agency is not aware, however, of any data which indicate that the use of respirators in high temperature situations results in "more immediate and dangerous hazards than exposure to the chemical."

With respect to oxyfluorfen specifically, the Agency believes (as stated in the PD 1/2/3) that its exposure estimates for applicators are, of necessity, "worst case" values and has invited the registrant to submit data demonstrating that actual exposure to PCE is significantly lower than Agency estimates. These data are not anticipated to be costly to generate and could successfully rebut the respirator requirement. Until such time as these data are available or other protective methods are developed, the Agency will require the currently available means of reducing inhalational exposure (respirators) to be used during mixing, loading, and application of oxyfluorfen products.

The registrant has also submitted comments (30000/36:#1) on implementation of the respirator requirement. Rohm and Haas believes that "the actual inhalation exposure to PCE from Goal® formulations is significantly less than that calculated by the Agency and the company will obtain actual field monitoring data to substantiate its contention."

After reviewing comments from the Department of Agriculture, the Scientific Advisory Panel, and the registrant on the Agency's findings and recommendations concerning oxyfluorfen as set forth in the PD 1/2/3, the Agency has decided to implement its proposed decision without modification.

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APPENDIX A

Revised Exposure and Risk Tables from the Oxyfluorfen Position Document 1/2/3

TABLE 2.

Daily PCE Inhalation Exposure for Applicator/Mixer/Loaders Using Goal 2E[a/][b/]

CROP	(mg/kg bw/day)
Soybeans	5.282×10^{-3}
Field Corn	21.127×10^{-3}
Tree Fruits/Nuts	21.127×10^{-3}
Conifers	21.127×10^{-3}

a/ Assumes 200 ppm PCE in Goal 2E.

b/ Assumes an 8-hour day of spraying.

TABLE 3.

Daily PCE Dermal Exposure for Applicator/Mixer/Loaders Using Goal 2E[a/][b/][c/]

CROP	(mg/kg bw/day)
Soybeans	0.78×10^{-4}
Field Corn	6.20×10^{-4}
Tree Fruits/Nuts	0.83×10^{-4}
Conifers	3.10×10^{-4}

a/ Assumes 200 ppm PCE in Goal 2E.

b/ Assumes 1-hour mixing/loading and 7-hour spraying.

c/ Based on Staiff, et al. (1975) work on paraquat.

TABLE 4.

Adjusted Lifetime Average Daily Worker Exposure to PCE from Use of Goal 2E[a/]

Crop	Inhalation mg/kg bw/day	Dermal mg/kg bw/day	Total mg/kg bw/day
Soybeans	0.8×10^{-4}	1.2×10^{-6}	0.8×10^{-4}
Field Corn[b/] [1981]	20.6×10^{-4}	60.0×10^{-6}	21.0×10^{-4}
Tree Fruit/Nuts	3.3×10^{-4}	1.3×10^{-6}	3.3×10^{-4}
Conifer	3.3×10^{-4}	4.8×10^{-6}	3.4×10^{-4}

a/ Assumes 200 ppm PCE in Goal 2E.

b/ Soybean, tree fruit/nuts, and conifer estimates are based on 10 working days per year. Field corn estimates were further adjusted to reflect the number of days that applicators are estimated (Petrie, 1980c) to be treating field corn as part of the USDA Witchweed Eradication Program during 1981 (62.5 days). It is estimated that 100,000 acres of field corn will be treated in 1981.

TABLE 5.

Adjusted Lifetime Average Daily Worker Exposure
to PCE from Use of Goal 2E - Protective Clothing Scenario[a/]

Crop	Inhalation mg/kg bw/day	Dermal mg/kg bw/day	Total mg/kg bw/day
Soybeans	0	1.8×10^{-7}	1.8×10^{-7}
Field Corn [1981]	0	88.0×10^{-7}	88.0×10^{-7}
Tree Fruit/Nuts	0	1.9×10^{-7}	1.9×10^{-7}
Conifer	0	7.0×10^{-7}	7.0×10^{-7}

a/ Assumes applicators wear protective clothing and suitable respirator.

TABLE 9.

Carcinogenic Risk to Applicator/Mixer/Loaders and to the General Population Associated with the PCE Contaminant of Goal 2E (Dykstra, 1981b)

Crop	Exposure Estimate (mg/kg/day)	Risk Estimate
Worker:		
Soybeans	0.8×10^{-4}	4.2×10^{-6}
Field Corn	21.0×10^{-4}	1.1×10^{-4}
Tree Fruit/Nuts (bearing; nonbearing)	3.3×10^{-4}	1.7×10^{-5}
Conifers	3.4×10^{-4}	1.8×10^{-5}
Dietary:		
Soybeans	1.0×10^{-6}	5.30×10^{-8}
Field Corn	5.7×10^{-7}	3.03×10^{-8}
Tree Fruit/Nuts (bearing only)	1.9×10^{-5}	1.00×10^{-6}

TABLE 10.

Adjusted Lifetime Average Daily Worker Exposure to and Associated Risk from PCE in Goal[a/]

Crop	Inhalation (mg/kg bw/day)	Dermal (mg/kg bw/day)	Total (mg/kg bw/day)	Risk
Soybeans	0	1.8×10^{-7}	1.8×10^{-7}	9.5×10^{-9}
Field Corn [1981]	0	88.0×10^{-7}	88.0×10^{-7}	4.7×10^{-7}
Tree Fruit/Nuts	0	1.9×10^{-7}	1.9×10^{-7}	1.0×10^{-8}
Conifers	0	7.0×10^{-7}	7.0×10^{-7}	3.7×10^{-8}

a/ Assumes applicators wear protective clothing and suitable respirator.

TABLE 11.

Comparison of Applicator Risk With and Without the Use of Protective Equipment

Crop	Risk Without Protective Equipment	Risk When Protective Equipment is Employed
Soybeans	4.2×10^{-6}	9.5×10^{-9}
Field Corn [1981]	1.1×10^{-4}	4.7×10^{-7}
Tree Fruit/Nuts	1.7×10^{-5}	1.0×10^{-8}
Conifers	1.3×10^{-5}	3.7×10^{-8}

The Following Tables and Sample Calculations Are Revisions of Appendix A of the Oxyfluorfen Position Document 1/2/3, pp. 96-101.

Maximal PCE Applied Under Goal 2E Use Conditions[a/]

	Application Rate			
	Goal (lb/A)		Perchlorethylene	
	Pounds A.I. per acre	Gallons Goal^{R}2E per acre	lb/acre[b/]	gm/acre[c/]
Soybeans	0.5	0.25	0.00042	0.19
Field Corn	2.0	1.00	0.00167	0.76
Tree Fruit/Nuts	2.0	1.00	0.00167	0.76
Conifers	2.0	1.00	0.00167	0.76

a/ Rohm and Haas, 1978. p. 580 (modified). Assumes 200 ppm PCE in Goal^{R}2E.

b/ 8.34 lb./gallon/acre x $2 \times 10^{-4} = 1.67 \times 10^{-3}$ lb PCE/acre.

c/ 1.67×10^{-3} lb PCE/acre x 454 gm/lb. = 0.76 gms PCE/acre.

Goal 2E and PCE Spray Rates, by Crop[a/]

Crop	Goal Spray Rate		PCE Spray Rate		
	Volume (gal./acre)	Weight[b/] (gm/acre)	Weight (gm/acre)	Concentration (gm/mg H_2O)	(ppm)
Soybeans	20	7.57×10^4	0.19	2.51×10^{-6}	2.5
Field	10	3.79×10^4	0.76	20.05×10^{-6}	20.1
Tree Fruit/Nuts	75	2.84×10^5	0.76	2.68×10^{-6}	2.7
Conifers	20	7.57×10^4	0.76	10.04×10^{-6}	10.0

a/ Rohm and Haas, 1978 (modified). Assumes 200 ppm PCE in Goal 2E.

b/ 1 gallon of H_2O weighs 8.34 pounds.

2. Sample calculations for inhalational, dermal, dietary exposure estimates.

$$\text{Inhalational Exposure (soybeans)} = \frac{\text{grams PCE/acre x volume air inhaled/day}^{a/}}{\text{volume of air/acre}^{b/} \text{ x average body weight}}$$

$$= \frac{0.19 \text{ gm PCE/acre} \times 14.400 \text{ liters/day} \times 1000 \text{ mg/gm}}{7.4 \times 10^{6} \text{ liters/acre} \times 70 \text{ kg body weight}}$$

$$= 5.282 \times 10^{-3} \text{ mg/kg bw/day}$$

a/ $1.8 \text{ m}^3 \text{ hr} \times 1000 \text{ l/m}^3 \times 8 \text{ hr/day} = 14.400 \text{ liters/day}$

b/ volume of air/acre = $6 \text{ ft} \times 43{,}560 \text{ ft}^2 \text{ acre} \times 28.3 \text{ l/ft}^3$

$= 7.4 \times 10^{6}$ liters of air/acre

$$\text{Dermal Exposure (soybeans)} = \frac{\text{PCE concentrations in diluted spray} \times \text{diluted spray contacting skin} \times \text{weight per pint of water} \times \text{percent Skin penetration}}{\text{average body weight}}$$

$$= \frac{2.51 \text{ ug/g} \times 0.048 \text{ pints}^{a/} \times 454 \text{ g/pint} \times 0.1^{a/} \times 1 \text{ mg/1000 ug}}{70 \text{ kg bw}}$$

$$= 7.8 \times 10^{-5} \text{ mg/kg bw/day}$$

a/ Values for the amount of liquid contacting applicator's skin (0.048 pints) and percentage skin penetration (10%) were estimated by the registrant (Rohm and Haas, 1978).

Appendix B

The comments of the Scientific Advisory Panel and the United States Department of Agriculture on the Preliminary Notice of Determination Concluding the Rebuttal Presumption Against Registration of Pesticide Containing Oxyfluorfen are presented below in their entirety.

FEDERAL INSECTICIDE, FUNGICIDE, AND RODENTICIDE ACT (FIFRA)

SCIENTIFIC ADVISORY PANEL

Review of Preliminary Notice of Determination
Concluding the Rebuttable Presumption Against
Registration (RPAR) of Pesticide Products Containing
Oxyfluorfen (GOAL 2E)

The Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) Scientific Advisory Panel has completed review of plans by the Environmental Protection Agency (EPA) for initiation of regulatory action on pesticide products containing oxyfluorfen (GOAL 2E) under the provisions of Section 6(b)(2) of FIFRA, as amended. The review was completed in an open meeting held in Arlington, Virginia on March 13-14, 1981. The following Panel members were present for the review: Drs. Torgeson, Doull, Metcalf, and Davies.

Maximum public participation was encouraged for the review. Public notice of the meeting was published in the Federal Register on Wednesday, April 27, 1981. In addition, telephone calls were received from and mailings sent to the general public who had previously expressed an interest in activities of the Panel.

Written and oral statements were received from technical staff and representatives of the Environmental Protection Agency. A written statement was received from Rohm and Haas Company, the registrant for oxyfluorfen. Company representatives also participated extensively in the discussion.

In consideration of all matters brought out during the meeting and careful review of all documents presented by the Agency and other parties, the Panel unanimously submits the following report:

Scientific Advisory Panel Report on
Oxyfluorfen (GOAL 2E)

The Panel concurs with the Agency's proposed decision to conclude the Rebuttable Presumption Against Registration (RPAR) of Oxyfluorfen (GOAL 2E) on the grounds that the oncogenic hazard from perchloroethylene (PCE) contained in the compound is no longer sufficient to warrant the denial of a conditional registration for various uses.

However, the Panel has a number of serious concerns with oxyfluorfen not related to the oncogenic hazard of PCE and wishes to bring these to the attention of the Agency. These concerns are:

1. The persistence of oxyfluorfen and its possible bio-magnification in the food chain. This concern is based on Japanese data on related compounds which indicate a bioaccumulation effect.

2. The adequacy of testing of oxyfluorfen's potential teratological effects. The Panel expresses the belief that it is necessary to make special efforts to determine that no teratological problems exists with all the diphenyl ether class of chemicals. The Panel thus recommends that additional teratological testing be conducted, with e.g. nitrofen being used for a positive control as a comparison.

3. The identification of the various inert ingredients in oxyfluorfen and their potential adverse effects on the environment. The Panel notes that there is an impurities level of 28 percent in oxyfluorfen technical material, and states its belief that considerably more information is needed on the potential effects of these impurities.

The Panel further notes that although oxyfluorfen is intended initially as a specialty herbicide with relatively low usage planned, nonetheless, the potential exists for much greater use, e.g. as a replacement for nitrofen, and therefore one must be concerned over potential health effects on a broader scale.

In conclusion, the Panel recommends that monitoring studies be designed and carried out in order to clarify any adverse environmental effects of the use of oxyfluorfen.

FOR THE CHAIRMAN:

Certified as an accurate Report of Findings:

Philip H. Gray, Jr.
Executive Secretary
FIFRA Scientific Advisory Panel

DATE: June 19, 1981

July 6, 1981

Mr. Edwin L. Johnson (TS-766C)
Acting Deputy Administrator for
Pesticide Programs
U. S. Environmental Protection Agency
Washington, D. C. 20460

Dear Ed:

This is the U. S. Department of Agriculture's response to the U. S. Environmental Protection Agency's (EPA) Preliminary Notice of Determination Concluding the Rebuttable Presumption Against Registration of the pesticide chemical oxyfluorfen (GOAL).

We concur with the Agency's conclusions that the benefits from the use of this chemical are biologically and economically meaningful to agricultural production. We have used Goal in our witchweed program over the past three years. Where it has been used, control of witchweed has been excellent lasting from six weeks to full season without observable adverse effects on corn or other aspects of the environment. Goal is rated as the best of the new herbicides for use in forest nurseries. The indications are that it will become a very important tool because it can be applied over the top of five-week old seedlings without any noticeable phytotoxicity and because of the season-long control the material provides.

We agree with the requirement to use a respirator during the mixing, loading and application of oxyfluorfen until the registrant can more accurately assess inhalation exposure; however, we are concerned that the requirement for respirators makes no differentiation between methods of application. In many forest nurseries, pesticides are applied through automatic watering systems which would result in little or no applicator exposure. In less sophisticated nurseries the material is applied with a directed spray which should result in low inhalation exposure. We are hopeful that the additional toxicology studies that the agency has requested from the registrant will demonstrate that the use of respirators is not necessary. If it is determined that the use of respirators is necessary, we suggest that consideration be given to evaluating protective equipment that poses minimal discomfort in hot, humid climate. As we have pointed out in the past, the use of respirators in many areas of the U. S. poses problems of discomfort due to heat and humidity. In these climatic conditions applicators and other support personnel are often reluctant to use them, regardless of regulatory requirements. It has been suggested that in certain high temperature situations the hazards associated with the use of respirators may be more immediate and dangerous than the hazard due to chemical exposure which the use is intended to prevent.

We would recommend followup action that would substantiate that respirators significantly lower exposure during application and that they are mitigating the problem. Research is needed to devise protective measures suitable for hot weather.

If we can be of assistance in developing needed exposure data, please advise.

Sincerely,

Barry R. Flamm
Director